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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No.: 09/776,533

Group Art Unit: 1644

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JUN 13 2003

Filed: February 7, 2001

Examiner: Phillip Gambel

PETITIONS OFFICE

For: *MODULATION OF VASCULAR HEALING BY INHIBITION OF  
LEUKOCYTE ADHESION AND FUNCTION*Assistant Commissioner for Patents  
Washington, D.C. 20231**SECOND REQUEST FOR RECONSIDERATION OF DECISION  
BY THE GROUP DIRECTOR OF RESTRICTION REQUIREMENT**

Sir:

Pursuant to 37 C.F.R. § 1.144, applicants petition the Commissioner to review the restriction requirement set forth in the Decision on Petition dated May 28, 2003, revising the restriction requirement made in the Office Action mailed June 11, 2002, made final in the Office Action mailed September 6, 2002. No fee is believed to be due.

**The June 11, 2002 Restriction Requirement**

The Office Action mailed June 11, 2002, divided the claims into 24 groups. These are appended for the convenience of the Commissioner in Appendix A.

In the response filed July 11, 2002, applicants elected for prosecution group I,

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claims 1-12, and elected with traverse the species of Mac-1-specific antibodies. Claims 13-17 were cancelled. A petition for review of the restriction requirement was filed on October 4, 2002, and denied in the decision mailed December 18, 2002.

### **The Restriction Requirement in the Parent Application**

As previously noted, this application is a continuing application of 08/823,999 filed March 5, 1997, to which this application claims priority. In prosecution of the parent application, a restriction requirement was imposed by the *same examiner* (See Appendix B), where the *same claims* were divided into only two groups, and an election of species was made. This application was not only prosecuted on this basis, but was appealed on this basis, with data and arguments submitted during prosecution and on appeal that were based on the original restriction requirement. The Board of Appeals has already rendered a decision in the parent case based on the same claims as originally presented. These arguments are prejudicial to any prosecution by applicants that would have to be made in the present application based on the current restriction requirement.

### **The Restriction Requirement in the Decision on Petition**

The decision mailed May 28, 2003, rewrites the restriction requirement but in an equally improper manner. Claims 1-4, 11 and 12 are acknowledged as generic claims. The decision, however, then says that since there are allegedly patentably distinct species defined within the claims, and that the examiner has already determined the

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generic claims are unpatentable (note this is based solely on a first office action), then it is appropriate to restrict claims 5, 6, 9 and 10 into nine groups, and claim 8 into three groups. Note that claim 5 is divided into four different inventions, and claim 9 is divided into four different inventions.

Claims must be both patentably distinct and independent in order to be subject to restriction requirement. Definitions are provided by CHISUM 4:12.03[1]: The Patent and Trademark Office defines "independent" as meaning "not dependent," which in turn means "there is no disclosed relationship between the two or more subjects disclosed." Examples include species not usable together as disclosed or process and apparatus incapable of being used in practicing the process. The Office cites the extreme example of a shoe and a locomotive bearing. The Office defines "distinct" as meaning related or dependent but "capable of separate manufacture, use or sale as claimed" and "patentable over each other." Examples of dependent and distinct inventions include combination and subcombination, process and apparatus, process and product, and composition and process of use under appropriate circumstances.

In an election of species, only the elected species is initially examined. Once this claim is determined to be allowable, the examiner must search the remaining species. The claimed methods are related because they all have (1) a common mechanism of action; (2) a common target; and (3) a common result, i.e., "decreasing or inhibiting integrin-mediated stenosis or restenosis or a blood vessel".

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Further, the MPEP states that species, "while usually independent, may be related under the particular disclosure. Where inventions as disclosed and claimed are both (A) species under a claimed genus and (B) related, then the question of restriction must be determined by both the practice applicable to election of species and the practice applicable to other types of restrictions such as those covered in MPEP 806.05-806.05(i)." (MPEP 806.04(b))

The relationship between species is disclosed. Compounds that inhibit leukocyte adherence by inhibiting integrins or integrin ligands as stated on page 7 line 26 to page 8 line 6. The claimed method is directed to *a method of inhibiting stenosis or restenosis by inhibiting integrin-mediated cell adhesion*. Clearly blocking different members of the integrin family or an integrin ligand is encompassed by the scope of this method. "Current Patent and Trademark Office policy precludes restriction, even in the case of multiple species, unless the two groups of claims are patentable over each other (*i.e.*, neither is obvious in the light of the other) (Chisum 4:12.03).

The similarity of the members of the different groups is further demonstrated by the fact that they only belong to two class/subclass combinations. In the restriction requirement of the parent application, the examiner stated that the integrins and their receptors constituted distinct species because their structures and modes of action are different. Mac-1, LFA-1, p150,95, and CD11d/CD18 are all integrins. The ligands for these integrins overlap.

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The present specification describes a relationship of the integrins all being involved in leukocyte adhesion (page 7, lines 16-21), and where the integrin ligands show promiscuity by binding to multiple integrins (page 7, lines 21-25). The specifically different embodiments of the invention are defined in proper Markush groups. "Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility" *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984).

The integrins all share a common utility of binding extracellular matrix. They are also composed of two non-covalently associated transmembrane glycoprotein subunits  $\alpha$  and  $\beta$ , both of which contribute to binding the matrix. This structural feature is essential to the utility. Unity of invention exists. Blocking any of the disclosed receptors or ligands will inhibit leukocyte adhesion to prevent stenosis/restenosis.

The same examiner has already searched the group consisting of claims 1-12 with the same elected species in the parent application. It can hardly represent an additional burden to conduct the exact same search in the continuation application.

The MPEP provides that if an applicant discloses multiple species but includes only generic claims, election between species is normally not required. If an applicant discloses multiple species and includes claims restricted to those species, the applicant will be required to elect one species. He will then be restricted to those claims that

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read on that elected species unless a generic claim is found to be allowable. In the latter event, the applicant may include further claims to additional species (up to a reasonable number) provided that such additional claims "are written in dependent form (Rule 75), or otherwise include all the limitations of the generic claim."

This is exactly the situation here. Claim 1 is generic. In the restriction requirement of the parent application, the examiner stated that claim 1 and claim 13 (now cancelled) are proper generic claims. It is inconsistent for a generic claim previously satisfying the requirements of MPEP 806.04(d) to be deemed not generic at a later date.

The restriction requirement, by creating separate inventions out of the generic claim, makes it impossible to examine claim 1 in its entirety, and forces the applicants to restrict it to a single species.

The examiner has no legal authority to require applicants to restrict a generic claim to a single species, absent prior art or lack of enablement.

The parent case, based on the claims as originally restricted by this same examiner, has been examined by this same examiner, evidence submitted, and is now on appeal. It would unfairly prejudice the Applicants to make a restriction requirement of the same claims which have already been prosecuted and which are now waiting at the Board of Appeals. Arguments have been made arguing results with one species are predictive of results with another species, all of which are joined by a common function

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(i.e. the inhibition of leukocyte adhesion and function). It is well established that a genus can be linked by a common function, to achieve a common result: in this case, modulation of vascular healing, and in particular, prevention or mitigation of restenosis.

In *Mark I Marketing Corp. v. R.R. Donnelley & Sons Co.* (1995), 154, the Federal Circuit stressed that " 'The prosecution history must be examined as a whole in determining whether estoppel applies.' "; "Thus, the relevant prosecution history here includes not only the ... application [upon which the patent issued] but also the parent ... and grandparent ... applications. Chisum 5A:18.05[2][d][ii]"

The Examiner should be bound by the final decisions he rendered during the prosecution of claims 1-12 as a single invention in the parent application. These claims have been prosecuted together as a group under the same prior art references in office actions of the parent. The previous history of prosecuting this group of claims as one invention acknowledges that they are related. It is inconsistent to restrict the exact same claims differently in this application than in the parent application.

### Summary

The current restriction imposed on the claims of the present invention is improper. This restriction is inconsistent with the guidelines for restriction practice delineated by the MPEP. The claims of this invention are directed to the method for inhibiting stenosis or restenosis. Upholding this restriction requirement would be to allow the examiner to impose limitations on the claims *which are not now present*.

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Favorable consideration of this petition is earnestly solicited.

Respectfully submitted,



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Pam Turnbough

Date: June 13, 2003



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**APPENDIX A:**      *Clean Copy of Claims as Pending*

1.      A method of inhibiting or reducing stenosis or restenosis of a blood vessel following injury to vascular tissue in a region of the blood vessel of a patient in need of treatment thereof, comprising:

administering systemically or at the site of the injury a pharmaceutically acceptable composition comprising a compound which specifically inhibits or reduces leukocyte integrin-mediated adhesion or function in an amount effective to inhibit or reduce stenosis or dependent restenosis of a blood vessel following injury to vascular tissue.

2.      The method of claim 1 wherein the leukocytes are monocytes or granulocytes.

3.      The method of claim 1 wherein the injury arises from angioplasty, atherectomy, endovascular stenting, coronary artery bypass surgery, peripheral bypass surgery, or transplantation of cells, tissue or organs.

4.      The method of claim 1 wherein the composition is in a form selected from the group consisting of solutions, gels, foams, suspensions, polymeric carriers, and liposomes.

5.      The method of claim 1 wherein the integrin is selected from the group consisting of Mac-1, LFA-1, p150,95, and CD11d/CD18.

6.      The method of claim 5 wherein the integrin is Mac-1.

7.      The method of claim 6 wherein the ligand is selected from the group consisting of ICAM-1, fibrin(ogen), C3bi, and factor X.

8.      The method of claim 1 wherein the compound is selected from the group

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consisting of antibodies and antibody fragments that are immunoreactive with integrins or their ligands and which block the interaction of the integrins or their ligands with vascular cells; molecules which inhibit expression of the integrins or their ligands, and peptides and peptidomimetics derived from the integrins or their ligands which block the interaction of the integrins or their ligands with vascular cells or tissues.

9. The method of claim 5 wherein the integrin is LFA-1 and the ligand is selected from the group consisting of ICAM-1, ICAM-2, ICAM-3.

10. The method of claim 6 wherein the compound is an antibody or antibody fragment immunoreactive with Mac-1.

11. The method of claim 1 wherein the compound is administered to a patient in need thereof prior to vascular intervention.

12. The method of claim 11 wherein the compound is administered to a the patient prior to and after vascular intervention, until healing has occurred.

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